

U.S. Patent Application Serial No. 09/340,196
Amendment dated August 21, 2003
Reply to OA of May 21, 2003

REMARKS

Claims 51, 53, 54, 56, 59 and 68-77 are pending in this application. Amendments are proposed to claims 51, 53, 56, 59 and 68-75.

A personal interview between Examiner Holleran and Daniel Geselowitz was held on August 20, 2003. In the interview, possible amendments to clarify the last clause of claim 51 and the other independent claims was discussed in regard to the relationship of the claims to the Declaration under 37 CFR 1.132, pertinent to the rejections under 35 U.S.C. 103(a). The enablement rejection under 35 U.S.C. 112, first paragraph, was also discussed.

The rejection of claims 51, 53, 54, 56, 59, 68, 69, 73, 74 and 77 under 35 U.S.C. 103(a) as being unpatentable over Yamamoto (Yamamoto et al. Eur. J. Biochem. 143:133-144, 1984) in view of Benita (Benita et al. Eur. J. Nucl. Med. 6:515-52, 1981) and further in view of Canfield (WO 87/00289) is maintained (Office action paragraph 6).

Reconsideration of the rejection is respectfully requested in view of the proposed amendments to the claims.

In the rejection, the Examiner indicates that the Declaration under 37 CFR 1.132 was not commensurate in scope with the claims. In particular, the Examiner states on page 3:

“This argument is unpersuasive, because the claims are not limited to differentiating between malignant tumors and benign thyroid tumors, and the claims include within their scope methods for differentiating between

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malignant thyroid tumors and normal thyroid.”

Applicants submit that the Examiner’s position resulted from a misunderstanding of the intended scope of the claims. Applicants have clarified the recitations of all of the pending claims by amending the last clause of the independent claims to read as follows:

“wherein the sample is determined to be malignant when the calculated ratio is significantly higher or lower than that of the reference fluid sample of the normal thyroid and is significantly higher or lower than that of the reference fluid sample of the benign thyroid.”

This amendment clarifies that the determination of malignancy is made by comparing the sample **both** to reference normal thyroid and to reference benign thyroid. Applicants submit that this amendment represents clarification of the claim and does not represent new matter. Support for the amendment may be seen in the specification on page 26, second paragraph, to page 27, second paragraph. Page 26, second paragraph, for example, reads: “...malignancy of thyroid tumor, in other words, as to whether the tumor is benign or malignant thyroid carcinoma, can be determined.” The first full paragraph on page 27 discloses specific examples of using differential Tg binding to distinguish papillary carcinoma from benign thyroid adenoma, papillary carcinoma from Grave’s disease and normal, and so on. The specification on page 38, last paragraph, summarizes that the method allows: “differentiation of papillary carcinoma from benign thyroid adenoma and differentiation of follicular carcinoma from adenoma can be conducted by **using a suitable combination of measurements results of various kinds of Tg(s)**” (emphasis added).

Applicants therefore submit that the pending claims, as amended, are commensurate in scope with the Declaration under 37 CFR 1.132, demonstrating unexpected results for the present

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invention, and that the pending claims are therefore novel and non-obvious over Yamamoto (Yamamoto et al. Eur. J. Biochem. 143:133-144, 1984), Benita (Benita et al. Eur. J. Nucl. Med. 6:515-52, 1981) and Canfield (WO 87/00289), taken separately or in combination. Entry of the amendments and withdrawal of the rejection are respectfully requested.

The rejection of claims 51, 53, 54, 56, 59, 68, 69, 73, 74 and 77 under 35 U.S.C. 103(a) as being unpatentable over Tarutani (Tarutani et al. Biochem. 98:851-857, 1985) in view of Benita and further in view of Canfield is maintained (Office action paragraph 7).

Reconsideration of the rejection is respectfully requested in view of the proposed amendments to the claims. Applicants have discussed above the rejection under 35 U.S.C. 103(a) over Yamamoto et al., Benita and Canfield. Applicants respectfully submit that the citation of Tarutani instead of Yamamoto et al. does not further provide a suggestion or motivation for the rejected claims, and does not provide any teaching contradicting Applicants' contention that the results in the Declaration under 37 CFR 1.132 are unexpected. Entry of the amendments and withdrawal of the rejection are respectfully requested.

The rejection of claims 70-72, 75 and 77 under 35 U.S.C. 103(a) as being unpatentable over Tarutani or Yamamoto in view of Benita and Canfield, and further in view of Robbins (U.S. Patent No. 5,902,725) is maintained (Office action paragraph 8).

Reconsideration of the rejection is respectfully requested in view of the proposed

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amendments to the claims. Applicants have discussed above the rejection under 35 U.S.C. 103(a) over Yamamoto et al., Benita and Canfield. Applicants respectfully submit that the additional citation of Tarutani and the citation of Robbins do not further provide a suggestion or motivation for the rejected claims, and does not provide any teaching contradicting Applicants' contention that the results in the Declaration under 37 CFR 1.132 are unexpected.

Applicants note that the Examiner also states that Applicants argued that "teachings of Robbins cannot be extrapolated to the claimed invention because Robbins teaches a PSA assay." Applicants respectfully submit that they did **not** argue that. With regard to Robbins, Applicants argued specifically only that Robbins did not suggest the step of determining malignancy based on the calculated ratio. That is, Robbins does not provide any further suggestion for this step in the combination of references.

Again, entry of the amendments and withdrawal of the rejection are respectfully requested.

The rejection of claims 51, 53, 54, 56, 59 and 68-77 under 35 U.S.C. 112, first paragraph, is maintained (Office action paragraph 9).

Reconsideration of this rejection is respectfully requested.

In the Office action, the Examiner indicates that Applicants' arguments were not directed at the basis for the rejection. The Examiner states:

"The basis for this rejection is that the specification provides no evidence that two types of thyroglobulin exist where one type has a Lewis type sugar chain and a second type lacks a Lewis type sugar chain, and that this differential glycosylation

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of thyroglobulin is associated with thyroid malignancy."

In response, Applicants respectfully maintain their previous arguments that one of skill in the art could readily practice the method of the invention. The Examiner appears to be saying, in effect, that Applicants **have** stated how to perform the method, but that Applicants **have not proven** that the method detects of malignancy with Lewis type sugar chains.

In response, Applicants submit that is has long been considered to be possible to patent completely hypothetical methods for which no experimental data are provided, as long as there is adequate written description and enablement. Applicants submit that the Examiner is here attempting to deny patentability based on a lack of certain working examples. However, Applicants have adequately described how the method would be carried out for these examples, and that Applicants have met the written description and enablement requirements.

Moreover, the Examiner states that Applicants' claims represent an "invitation to experiment". Applicants respectfully submit that this is not the case. The claims clearly recite what is to be done, and, in fact, **no undue experimentation is necessary to carry out the recitation of the claims.**

The Examiner indicates that "further research to establish the relationship between the presence of Lewis type sugar chains on species of thyroglobulin and thyroid cancer would be required" and that this would be "undue experimentation." However, the experimentation to which the Examiner refers would appear only to be testing different possible embodiments to see which is "better" in a medical sense. Applicants submit that this is **not** experimentation that is necessary in

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order to practice the invention.

Anytime a claim encompasses more than one embodiment, it is likely that one of the embodiments will be “better” than another. The fact that Applicants did not provide working examples of all possible embodiments of their invention does not mean that the untested embodiments are not enabled. Applicants also note that they believe that it is extremely common for medically related patents to be issued with claim scopes that cover embodiments that do not “pan out” as actual medicines or medical methods, and that this in no way means that these embodiments were not enabled.

Again, reconsideration of the rejection is respectfully requested.

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If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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